Attorney Docket No. 0450-0001
PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of: William Daniel HILLIS

Serial No.: 09/821,694

Group Art Unit: 1634

Filing Date: March 28, 2001

Examiner: Frank Wei Min LU

Title: METHOD AND SEQUENCES FOR DETERMINATE NUCLEIC ACID HYBRIDIZATION

REPLY TO RESTRICTION REQUIREMENT, SPECIES ELECTION, AND SEQUENCE RULE COMPLIANCE

Commissioner for Patents
Washington, D.C. 20231

Sir:

This is in reply to the Detailed Action including a Restriction Requirement, a Species Election, and a Sequence Rule Compliance for the above-identified application. The Detailed Action was mailed July 11, 2002. As this Reply is filed within the thirty day shortened statutory period for response, no extension of time is required. Applicant respectfully requests reconsideration of the restriction in light of the remarks set forth below.

REPLY TO RESTRICTION REQUIREMENT:

The Examiner has required restriction between six groups of claims:

Group I. Claims 1-39, drawn to a method of employing oligonucleotide probes to obtain information on a target nucleic acid analyte;

Group II. Claims 40-86, drawn to a method for analysis of a plurality of target nucleic acid sequences;

Group III. Claims 87 and 88, drawn to a method for determining a nucleotide at a position of interest in an analyte nucleic acid sequence;

Group IV. Claims 87-94 and 99-105, drawn to a collection comprised of probe nucleic acid sets;

Group V. Claims 95-98 and 106-109, drawn to an array comprising the probe nucleic acid sequences; and

Group VI. Claims 110-114, drawn to a probe system comprising a pair of probe nucleic acid sequences sets.

In response, Applicant provisionally elects the claims of Group 1, with traverse.

REPLY TO SPECIES ELECTION:

The Examiner has also required election between the following species:

Species covered by Generic Claims 1, 5-24, 27-40, 44-69, and 72-114:

(i) four nucleotides (claims 2, 25, 41, and 70); and

(ii) more than four nucleotides (claims 3-4, 26, 42-43, and 71)

Species covered by Generic Claims 1-6, 18-26, 34-35, 40-45, 56, 62-71, and 87-114:

(iii) the sequencing method by analysis of hybridization data obtained from an array of oligonucleotide probes (claims 7-16, 28-32, 36-39, 46-55, and 57-59);

(iv) the sequencing method is by detection of labels that attached to by hybridization to the target sequence segment (claims 17, 33, 60-61); and

(v) the sequencing method is by analysis of hybridization data obtained from an array of target nucleic acid analyte sequences attached to a substrate surface (claims 27 and 72-86);

Species covered by Generic Claims 1-9, 14-15, 17-31, 33-38, 55-57, and 60-114:

(vi) detection of a discrete label moiety linked to the target sequence segment (10-13 and 49-54); and

(vii) detection of the heat of hybridization (claims 16, 32, 58-59).

Applicant provisionally elects the species identified by (i), (iii), and (vi) above, without traverse.

SEQUENCE RULE COMPLIANCE:

Applicant received the original Notice to Comply for the above-identified application shortly after the December 3, 2001, mailing date of the Notice. Applicant timely replied to the original Notice on

February 4, 2002. A copy of the Response to the Notice to Comply, including the paper copy of the sequence listing and the stamped dated post-card indicating receipt of same by the USPTO is attached to this Reply. Upon the Examiner's Request, Applicant will provide the USPTO with another copy of the computer readable form of the sequence listing.

REMARKS

INTRODUCTORY STATEMENT:

This application was filed on March 28, 2001 with 114 claims. The Restriction Requirement at issue attempts to break the application into six separate inventions. Applicant submits that the instant application should *not* broken apart into more than *two* separate applications: one directed to the methods of claims 1-88 and the other directed to the products of claims 89-114. The following arguments demonstrate why the method claims should be kept together in one group and why the product claims should be kept together in another group.

As a preliminary matter, Applicant sets forth the MPEP guidelines for restriction requirements:

Section 803 of the MPEP provides that criteria for a proper restriction requirement are:

(A) Inventions that are independent or distinct when claimed; and

(B) A serious burden on the Examiner.

The MPEP explains that with any restriction requirement, Examiners must provide reasons and/or examples to support conclusions and that a serious burden on the Examiner may be *prima facie* shown by appropriate explanation of separate classification, separate status in the art, or a different field of search. *See also,* MPEP § 808.02.

THE METHOD CLAIMS

First, the Examiner argues that Groups I and II are distinct and independent inventions because the examination of the claims of Group II would require an additional search for the plurality of target nucleic acids, which would not be necessary in the examination of the claims of Group I. The claims of Group I and II are both identified as requiring a search under class 435, subclass 6 (inventions involving nucleic acids). Whenever claims are classified together, a restriction is only proper (i) when an explanation indicates recognition of separate inventive efforts by inventors or (ii) where it is necessary to search for one of the distinct subjects in places where no pertinent art to the other subject exists. MPEP § 808.02. Under this rubric, the Examiner has identified as a separate inventive effort requiring two separate searches, the steps to identify information on one nucleic acid (Group I) from the steps to analyze more than one nucleic acid (Group II). Applicant submits that the subject matter of the claims of Groups I and II is not so different as to warrant a restriction.

Accordingly, if the restriction between the claims of Groups I and II is to be maintained, Applicant respectfully requests an explanation on why methods of identifying information on one nucleic acid and methods of identifying information on a plurality of nucleic acids involves a recognized separate inventive effort by inventors or requires non-overlapping searches.

Second, the Examiner argues that Groups I and III are distinct and independent inventions because the examination of the claims of Group I would require an additional search for the lack of mismatch at the probed position, which would not be necessary in the examination of the claims of Group III. The claims of Group I are classified under class 435, subclass 6 (inventions involving nucleic acids) and the claims of Group III are classified under class 435, subclass 94 (inventions produced by the action of an isomerase). The claims of Group III (claims 87 and 88) are directed to a "method for determining a nucleotide at a position of interest in an analyte nucleic acid sequence having a target segment...wherein hybridization...occurs only if complementarity exists between the nucleotide at the position of interest and the nucleotide at the corresponding position." Claims 87 and 88 do *not* recite the use of an isomerase to achieve the methods claimed therein. Accordingly, it appears that the classification of the claims of Group III in class 435, subclass 94 is not proper.

Even assuming *arguendo,* that the classification of the claims of Group III is proper, the restriction requirement between the claims of Groups I and III still appears improper for the following reason. Claims are classified in a different class when each distinct subject has (i) attained recognition in the art as a separate subject for inventive effort *and* (ii) requires a separate field of search. MPEP § 808.02. Accordingly, with this restriction requirement, the Examiner is identifying a method to identify a target nucleic acid with no mismatch at the probed position (Group I) as a distinct invention from a method to determine the position of a nucleotide with complementary probes (Group III). Applicant submits that the subject matter of the claims of Groups I and III is not so different as to warrant a restriction.

Accordingly, if the restriction between the claims of Groups I and III is to be maintained, Applicant respectfully requests an explanation why hybridization methods with no mismatch at the probed position and hybridization methods with complementary probes have attained recognition in the art as separate subjects for inventive effort requiring separate fields of search.

Third, the Examiner argues that Groups II and III are distinct and independent inventions because examination of the claims of Group II would require an additional search for the plurality of target nucleic acids, which would not be necessary in the examination of the claims of Group II. The claims of Group II are classified under class 435, subclass 6 and the claims of Group III are classified under class 435, subclass 94. As provided above, Applicant believes that the claims of Group III have been misclassified.

Nevertheless, the Examiner provides no reason why the claims of Group II and III require searches in a different subclass and distinguishes the two groups only by the feature of the plurality of target nucleic acids, the same feature which is used to distinguish the claims of Groups I and II, which are both in the same subclass.

Accordingly, if the restriction between the claims of Groups I and III is to be maintained, Applicant respectfully requests an explanation on why methods of identifying information on one nucleic acid and methods of identifying information on a plurality of nucleic acids involves a recognized separate inventive effort by inventors or requires non-overlapping searches.

THE PRODUCT CLAIMS:

First, the Examiner argues that Groups IV and V are distinct and independent inventions because examination of the claims of Group V would require an additional search for the substrate surface, which would not be necessary in the examination of the claims of Group IV. Group IV is classified in class 536, subclass 24.3 and Group V is classified in class 435, subclass 287.2.

Applicant submits that this restriction requirement violates the "subcombination essential to combination" rule set forth in MPEP § 806.05(c). There, the MPEP explains that if there is *no* evidence that a claimed combination AB_{sp} is patentable without the details of the claimed subcombination B_{sp}, restriction is *not* proper. Accordingly, because the substrate surface (A) of the claims of Group V (AB_{sp}) by itself is not patentable without the details of the claims of Group IV (i.e., the collection of claim 89 (B_{sp})), restriction between the claims of Group IV and V is not proper.

Second, the Examiner argues that Groups IV and VI are distinct and independent inventions because examination of the claims of Group VI would require an additional search for the position basepairing to a unique doubly degenerate set of nucleotides, which would not be necessary in the examination of the claims of Group IV. Groups IV and VI are both classified in class 536, subclass 24.3. Thus, with this restriction, the Examiner is asserting that base pairing with one complementary nucleotide and base pairing with two or three natural bases are subjects that are recognized as requiring separate inventive effort by inventors or that require non-overlapping searches. Applicant submits that the subject matter of the claims of Groups IV and VI is not so different as to warrant a restriction.

Accordingly, if the restriction between the claims of Groups IV and VI is to be maintained, Applicant respectfully requests an explanation why base pairing with one complementary nucleotide and base pairing with two or three natural bases involves a recognized separate inventive effort by inventors or requires non-overlapping searches.

Third, the Examiner argues that Groups V and VI are distinct and separate products because and examination of the claims of Group V would require an additional search for the substrate surface, which

would not be necessary in the examination of the claims of Group VI. Group V is classified in class 435, subclass 287.2 and Group VI is classified in class 536, subclass 24.3.

Applicant submits that the restriction between the claims of Groups V and VI is not proper for the same reason set forth above in the discussion traversing the restriction of the claims of Groups IV and V.

CONCLUSION

As set forth above, Applicant traverses the restriction between the method claims of Groups I, II, and III and traverses the restriction between the product claims of Groups IV, V, and VI. Based upon the foregoing arguments, Applicant respectfully requests that method claims 1-88 remain together in one group and that product claims 89-114 remain together in another group. Should the Examiner comply with this request, Applicant elects to pursue method claims 1-88 in this application and reserves the right to file a divisional application during the pendency of this application on product claims 89-114.

Applicant has elected the species indicated on page 2 of this Reply without traverse and has responded to the Sequence Rule Compliance with copies of previously filed documents. As noted above, Applicant will provide the Examiner with another copy of the computer readable form of the sequence listing upon request.

The Examiner is welcome to contact the undersigned at 650-330-4913 with any questions relating to this Reply or to the application in general.

Respectfully submitted,

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